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09/445,439	02/23/00	SABEL	B 10644-0001-2

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1616	6

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/445,439	Sabel et al.
Examiner	**Group Art Unit**
Michael Hartley	1616

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-40* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-29 and 31-40* is/are rejected.

☒ Claim(s) *30* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Claim Objections

Claim 30 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claim is not further limiting because it only states an intended use (e.g., medicinal use) for the composition claimed in its base claim. It is suggested that claim 30 is canceled.

Claim Rejections - 35 USC § 101

Claims 31-37 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions and methods wherein the substance is many of the substances (e.g., drugs) listed in *Markush* format in these claims, does not reasonably provide enablement for compositions and methods wherein the substance is "transmitter and their respective receptor agonists and receptor antagonists, their respective precursors and metabolites." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In particular, the specification fails to enable the skilled artisan to practice the invention without undue experimentation. As held by *ex parte Forman* (230 USPQ 546, BdPatApp & Int.) and *In re Wands* (8 USPQ 2d 1400, CAFC), there are several guidelines when determining if the specification of an application allows the skilled artisan to practice the invention without undue experimentation.

Amount of guidance present

The specification fails to provide any guidance for which transmitters may be useful and/or how such transmitters are acquired. The specification also fails to provide any guidance what respective agonists, antagonists, precursors and/or metabolites are useful or how such precursors, metabolites, etc. are prepared. One of ordinary skill in the art would be able, without undue experimentation, to determine what transmitters are useful, what is even considered to be a transmitter, as well as, an antagonist, agonist, precursor and metabolite thereof.

Absence of working example

The specification fails to provide any working examples relating to the making and/or using of any drug targeting system having any of these substances.

Nature of invention

The nature of the invention is a composition which is a drug targeting system and method of using thereof. However, the nature of this invention would require that the skilled artisan be aware of the specific drug which is being targeted. However, the specification does not provide any guidance on the types of substances that are encompassed as transmitters and especially fails to provide any guidance on what would constitute a precursor or metabolite thereof.

State of the prior art

The state of the prior art preparing drug targeting nanoparticles as instantly claimed, requires the type of drug be known. Since methods of making polymer nanoparticles requires polymerization techniques which may require heat, treatment with organic solvents, etc., the drug must be known so that the such methods of preparing will not destroy the activity of the drug. The state of the prior art concerning a transmitter and their respective receptor agonists and receptor antagonists, their respective precursors and metabolites, is not well understood, since the substances encompassed thereby are not an art-recognized class of drugs with known properties and chemical formulae.

Relative skill of those in the art

The relative state of those in the art would not enable the skilled artisan to practice the instantly claimed method wherein the substance is a transmitter and their respective receptor agonists and receptor antagonists, their respective precursors and metabolites, since it would amount to undue experimentation to test which possible transmitters, as well as, agonists, antagonists, precursors and metabolites thereof would be useful.

Unpredictability in the art

Given the diversity of transmitters, as well as, any precursor (e.g., which is not a well-defined term) or metabolites, etc., it would be very unpredictable to use such a transmitter or the derivatives thereof as claimed, as instantly claimed.

Breadth of the claims

The claims are broad, given that the transmitter and their respective receptor agonists and receptor antagonists, their respective precursors and metabolites, would encompass an almost unlimited number of compounds and the actual scope thereof is not clear, since the specification provides no guidance to which specific compounds encompassed thereby may be used.

It is suggested that "transmitter and their respective receptor agonists and receptor antagonists, their respective precursors and metabolites" is deleted from the instant claims to obviate this rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 7, 8, 11, 12, 15, 16, 22, 23, 27, 28, 31-37 and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

In the present instance, claim 2 recites the broad recitation "a diameter below 1,000 nm," and the claim also recites "preferably between 1 and about 1,000 nm" which is the narrower statement of the range/limitation.

In the present instance, claims 12 and 23 recite the broad recitation "carboxylic acid esters," and the claim also recites "preferably fatty acid asters of glycerol and sorbitol, even more

preferably . . . " which is the narrower statement of the range/limitation. Claim 12 also recites the broad recitation "fatty alcohol sulfates" and the claim also recites "preferably sodium salts of fatty acids . . . even more preferably sodium stearate . . . " which is the narrower statement of the range/limitation.

In the present instance, claims 36 and 40 recite the broad recitation "oral, intravenous, subcutaneous, intramuscular, intranasal, pulmonary or rectal route," and the claim also recites "preferably on the oral or intravenous route" which is the narrower statement of the range/limitation.

Regarding claims 7 and 27, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

In claims 7 and 27 the recitation of "transmitter and their respective receptor agonists and receptor antagonists, their respective precursors and metabolites" is indefinite because it is not clear what is encompassed by said recitation. One of ordinary skill in the art would not be readily appraised to the scope of such substances since these terms are not a well-defined group of therapeutic substances in which structure and function could be determined. Also, precursors and metabolites thereof are not definite because it is not known what type of precursors and/or metabolites are encompassed thereby. Thus, the scope of this recitation is not definite and the metes and bounds of the invention are not defined.

In claims 8 and 28, the definition of the diagnostic agent as "useful in the diagnosis in nuclear medicine and in radiation therapy" is confusing because this recitation does not make sense. It is not clear what the diagnosis in nuclear medicine is referring to, as diagnosis is usually directed toward a disease, not a type of medicine. Also, the definition of a diagnostic agent in terms of something used for medicine or therapy is confusing. It is suggested that the specific type of diagnostic agent is added to the claim to clarify (e.g., radionuclide, if this is what is intended).

Claims 11, 12, 22 and 23 contain the trademark/trade name Genapol^{R}, Bauki^{R}, Pluronic^{R} 68, etc. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a stabilizer and, accordingly, the identification/description is indefinite.

In claims 15 and 16 the recitation of "polymerizing, in a per se known manner" is indefinite because it is not clear what is meant by this recitation. For example, it is not clear what all is encompassed by a known manner and how the use of "per se" further defines such a known

manner. It is suggested that the specific methods of polymerization encompassed by the instant invention are inserted in place of said recitation to clarify.

Claims 31-37 provide for the use of a drug targeting system, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-29 and 31-40 are rejected under 35 U.S.C. 102(b) as being anticipated by any one of Kreuter (WO 95/22963) or Canal (EP 486959) or Dyatlov (WO 94/15590) or Hyon (EP 330180).

Kreuter discloses a drug targeting system comprising, nanoparticles of a polymeric material wherein the nanoparticles comprise a polymeric material, one or more physiologically effective substances (e.g., therapeutics or diagnostics) and one or more stabilizers, and a physiological acceptable carrier, see pages 1-11. The nanoparticles have a size range of 1 to 1000 nm, see page 9. The drug targeting system disclosed by Kreuter includes the same

components as instantly claimed. For example, polymeric materials are disclosed on page 9, the stabilizers on page 10 and the physiologically effective substances (e.g., drugs) on page 11. Methods of making the nanoparticles by polymerization of polymeric precursor with the drug and stabilizer are described, e.g., pages 9+. The drug targeting systems are used in methods of delivery various drugs to various tissues, including those within the nervous system and across the blood brain barrier, see page 11-13. The nanoparticles are administered via various routes, intravenously, orally, etc., see page 9.

Canal discloses a drug targeting system comprising, microparticles (e.g., includes nanoparticles) of a polymeric material wherein the microparticles comprise a polymeric material, one or more physiologically effective substances (e.g., therapeutics or diagnostics) and one or more stabilizers, and a physiological acceptable carrier, see abstract. The microparticles (or nanoparticles) may have a size range of 100+ nm (e.g., 0.1 um), see page 3, line 43. The drug targeting system disclosed by Canal includes the same components as instantly claimed. For example, polymeric materials are disclosed on page 4, lines 20-23, the stabilizers (e.g., jellifying agents, such as, polysorbates, etc.) on page 4, lines 23+, and the physiologically effective substances (e.g., drugs) on page 4, lines 5+. Methods of making the nanoparticles by polymerization of polymeric precursor with the drug and stabilizer are described, e.g., page 3. The nanoparticles are administered via various routes, intravenously, orally, etc., see page 5.

Dyatlov discloses a drug targeting system comprising, nanoparticles (e.g., nanocapsules) of a polymeric material wherein the nanoparticles comprise a polymeric material, one or more

physiologically effective substances (e.g., therapeutics or diagnostics) and one or more stabilizers, and a physiological acceptable carrier, see abstract. The nanoparticles have a size range of 20-150 nm, see page 1. The drug targeting system disclosed by Dyatlov includes the same components as instantly claimed. For example, the polymeric material is a polyalkylcyanoacrylate (e.g., see page 5), stabilizers (e.g., Pluronics, etc.) are listed on page 10, and the physiologically effective substances (e.g., drugs) on page 6+. Methods of making the nanoparticles by polymerization of polymeric precursor with the drug and stabilizer are described, e.g., pages 12+. The nanoparticles are administered via various routes, intravenously, orally, etc., see page 7, lines 26+.

Hyon discloses a drug targeting system comprising, nanoparticles of a polymeric material wherein the nanoparticles comprise a polymeric material, one or more physiologically effective substances (e.g., therapeutics or diagnostics) and one or more stabilizers, and a physiological acceptable carrier, see pages 1-11. The nanoparticles have a size range of 10 nm to 300 um, see page 3. The drug targeting system disclosed by Hyon includes the same components as instantly claimed. For example, the polymeric material is a polylactic acid, stabilizers (e.g., surfactants) are listed on page 5, line 40+, and the physiologically effective substances (e.g., drugs) on pages 3-4. Methods of making the nanoparticles by polymerization of polymeric precursor with the drug and stabilizer are described, e.g., pages 5-6. The nanoparticles are administered via various routes, see page 6.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-29 and 31-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Kreuter (WO 95/22963) or Canal (EP 486959) or Dyatlov (WO 94/15590) or Hyon (EP 330180), or any combination thereof.

Kreuter, Canal, Dyatlov or Hyon all disclose drug delivery systems as described above.

Although any one of Kreuter, Canal, Dyatlov or Hyon does not specifically teach all of the same polymeric materials, stabilizers and drugs as instantly claimed, it would have been obvious to substitute any of these components which are taught as interchangeably equivalents in the art as shown by Kreuter, Canal, Dyatlov or Hyon, thereby yielding the instant invention. One of ordinary skill in the art would have been motivated to employ any combination of known equivalent polymeric materials, stabilizers or drugs because the prior art teaches that such components are equivalents and may be substituted for one another to provide desired properties, e.g., solubility, stability, therapeutic effect, etc.

Specification

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Conclusion

No claims are allowed at this time.

Note: Copies of the references cited on the PTO-892 are not being furnished because these references were cited in the PCT application to which the present application is a 371. Applicant has already provided copies of these references in the instant application.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center Custom Service Center whose telephone number is (703) 308-1235.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Examiner Michael Hartley whose telephone number is (703) 308-4411. The examiner can normally be reached on Tuesdays through Fridays and on alternate Mondays from 7:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Diana Dudash, can be reached on (703) 308-2328. The fax phone number for this Group is (703) 308-4556.

Date: 07/05/2000

Michael G. Hartley
Patent Examiner
Art Unit 1616